

CLAIMS:

1. A bifunctional molecule, comprising:
an antibody or antigen-binding portion thereof and a
targeting agent, wherein:
- 5 the antibody specifically binds to an antigen in a protein that
binds to α_v integrin; and
 the targeting agent specifically binds to a cell surface protein
that activates the phosphatidylinositol 3 (PI3K) signaling pathway.
2. The bifunctional molecule of claim 1, wherein the targeting
10 agent or portion thereof triggers phosphatidylinositol-3-OH kinase (PI3K)
activation.
3. The bifunctional molecule of claim 1, further comprising a
linker that links the antibody or antigen-binding portion thereof to the
targeting agent.
- 15 4. The bifunctional molecule of claim 1 that comprises a fusion
protein.
5. The bifunctional molecule of claim 1 that comprises
chemically conjugated polypeptides.
6. The bifunctional molecule of claim 2, wherein the linker is a
20 single amino acid or a peptide.
7. The bifunctional molecule of claim 1, wherein the antibody
comprises a heavy chain or a portion thereof sufficient for antigen-binding
fused to the targeting agent.
8. The bifunctional molecule of claim 1, wherein the antibody
25 portion an Fab'2 fragment.
9. The bifunctional molecule of claim 1, wherein the antibody
portion comprises a sufficient portion of the variable regions of the heavy
and light chains for antigen recognition.
10. The bifunctional molecule of claim 1, wherein the antibody
30 comprises the sequence of amino acids set forth in SEQ ID No. 2 or SEQ
ID No. 6 or a sufficient portion thereof for antigen recognition.

11. The bifunctional molecule of claim 1, wherein the antibody comprises the sequence of amino acids set forth in SEQ ID No. 4 or a sufficient portion thereof for antigen recognition.

12. The bifunctional molecule of claim 1, wherein the antibody
5 portion is an Fab fragment.

13. The bifunctional molecule of claim 10, wherein the nucleic acid encoding the antibody portion selected from

(a) the coding portion of the sequence of nucleotides set forth in SEQ ID No. 1 or SEQ ID No.5;

10 (b) a sequence of nucleotides that comprises one or more degenerate codons of (a); and

(c) a sequence of nucleotides that hybridizes along its full length under conditions of high stringency to a sufficient portion of (a) or (b) to encode an antigen-binding portion of the antibody.

15 14. The bifunctional molecule of claim 11, wherein the nucleic acid encoding the antibody portion is selected from

(a) the coding portion of the sequence of nucleotides set forth in SEQ ID No. 3;

20 (b) a sequence of nucleotides that comprises one or more degenerate codons of (a); and

(c) a sequence of nucleotides that hybridizes along its full length under conditions of high stringency to a sufficient portion of (a) or (b) to encode an antigen-binding portion of the antibody.

15. The bifunctional molecule of claim 1, comprising the
25 sequence of amino acids set forth in any of SEQ ID Nos. 7-14 for specific binding to a targeted receptor.

16. The bifunctional molecule of claim 1, wherein the protein that binds to α_v integrin is a viral protein or a bacterial protein that interacts with α_v integrins for internalization of the respective virus or
30 bacteria.

- DRAFT ATTACHMENT
17. The bifunctional molecule of claim 16, wherein the virus is selected from adenovirus and adeno-associated virus.
18. The bifunctional molecule of claim 1, wherein the antibody or portion thereof specifically binds to the penton base of an adenovirus.
- 5 19. The bifunctional molecule of claim 1, wherein the antibody or portion thereof specifically binds to an antigen that includes an RGD motif.
20. The bifunctional molecule of claim 1, wherein the targeting agent comprises all or sufficient portion thereof of a protein that binds to
- 10 G-protein coupled receptors, oncogene product receptors, hormone receptors or cytokine receptors that employ the PI3 signalling pathway for signal transduction,
- wherein the sufficient portion thereof specifically binds to the cell surface receptor therefor and internalizes linked viral or bacterial particles.
- 15 21. The bifunctional molecule of claim 1, wherein the targeting agent comprises all or sufficient portion thereof of a protein that binds to G-protein coupled receptors that employ the PI3 signalling pathway for signal transduction,
- wherein the sufficient portion thereof specifically binds to the cell
- 20 surface receptor therefor and internalizes linked viral or bacterial particles.
22. The bifunctional molecule of claim 1, wherein the targeting agent comprises all or sufficient portion thereof of hormone or growth factor or cytokine,
- wherein the sufficient portion thereof is specifically bind to the cell
- 25 surface receptor therefor and internalizes linked viral or bacterial particles.
23. The bifunctional molecule of claim 6, wherein the targeting agent or portion thereof is a tumor necrosis factor (TNF), an fibroblast growth factor (FGF), an insulin-like growth factor (IGF) a colony stimulating factor (CSF), insulin or a serum cell factor (SCF).
- 30 24. The bifunctional molecule of claim 6, wherein the targeting agent or portion thereof is insulin, IGF-1, TNF- α , SCF, CSF, a PDGF, an

FGF, a heparin binding epidermal growth factor (HEGF), a VEGF or dimer thereof.

25. The bifunctional molecule of claim 6, wherein the targeting agent or portion thereof is TNF- α , IGF-1, SCF or EGF.

- 5 26. The bifunctional molecule of claim 1, wherein targeted cell surface protein is selected from among a PDGF receptor, an IGF-1 receptor, an EGF receptor, a member of the FGF receptor family, a TNF receptor, a CSF-1 receptor, an insulin receptor, an IGF-1 receptor, an NGF receptor, an IL-2 receptor, an IL-3 receptor, an IL-4 receptor, an IgM receptor, a CD4 receptor, a CD2 receptor, a CD3/T cell receptor, a G protein linked thrombin receptor, an ATP receptor, and an fMLP receptor.
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27. The bifunctional molecule of claim 1, wherein the targeted cell surface protein is selected from among tyrosine kinase receptors that, when activated, result in increased accumulation of PtdIns(3,4,5)P3, receptors associated with the src family non-receptor tyrosine kinases that stimulate PI3Ks phosphorylate phosphatidylinositol(3,4,5)P3 (PtdIns(3,4,5)P3) accumulation.

28. An isolated nucleic acid molecule(s), comprising a sequence of nucleotides that encodes the bifunctional molecule of claim 1.

- 20 29. A targeted delivery vector, comprising:
a bifunctional molecule of claim 1; and
a viral or bacterial vector.

30. The targeted delivery vector of claim 29, wherein the gene delivery vector encodes a therapeutic product.

- 25 31. The targeted delivery vector of claim 29, wherein the vector is an adenovirus vector.

32. The targeted delivery vector of claim 29, wherein the vector is a fiberless adenovirus vector.

- 30 33. The targeted delivery vector of claim 29, wherein the bifunctional molecule and viral or bacterial vector are complexed by

interaction of the antibody portion of the bifunctional molecule with a viral or bacterial surface protein.

34. The targeted delivery vector of claim 12, wherein the bifunctional molecule and viral or bacterial vector wherein the antibody
5 portion of the bifunctional molecule is covalently linked to the viral or bacterial surface protein.

35. An isolated nucleic acid molecule, comprising as sequence of nucleotides encoding the bifunctional molecule of claim 1.

36. A combination, comprising:
10 a delivery vector for delivering gene products to targeted cells; and

a bifunctional molecule of claim 1.

37. The combination of claim 36, wherein the bifunctional molecule and delivery vector for delivering gene products to targeted cells
15 are complexed.

38. A method of targeted gene therapy, comprising administering a combination of claim 36.

39. A method of targeted gene therapy, comprising administering a combination of claim 37.